REMARKS

Applicant has amended claim 1 such that it recites:

> 1. A method of producing a graft of ~~non-hematopoietic~~ muscle tissue in damaged or diseased tissue of a subject in need thereof, which comprises:
>
> a) isolating stem cells from the peripheral blood sample of donor by apheresis,
>
> (b) implanting a population of the isolated stem cells into the damaged or diseased tissue,
>
> whereby implantation of the stem cells produces a graft of ~~non-hematopoietic~~ muscle tissue in the damaged or diseased tissue.

Applicant has also amended claim 14 to recite,

> 14. A method of treating damaged or diseased striated muscle tissue of a subject by producing a graft of ~~non-hematopoietic~~ muscle tissue in the damaged or diseased striated muscle tissue
>
> (a) isolating stem cells from peripheral blood of a donor by apheresis, and;
>
> (b) implanting a population of the isolated stem cells said striated muscle tissue in need of treatment,
>
> whereby implantation of the stem cells produces a graft of ~~non-hematopoietic~~ muscle tissue in said striated muscle tissue."

And applicant has amended claim 31 to recite,

> 31. A method of treating an ischemic organ in a subject by producing a graft of ~~non-hematopoietic~~ muscle tissue in said ischemic organ, wherein said method comprises:
>
> (a) isolating stem cells from peripheral blood of a donor by apheresis, and;
>
> (b) implanting the isolated stem cells into the ischemic organ,
>
> whereby the implanted stem cells produce a graft of ~~non-hematopoietic~~ muscle tissue in the ischemic organ.

Support for these amendments is found on, e.g., page 4, lines 32 to 34, wherein applicant discloses:

> The implanted peripheral blood stem cells proliferate and differentiate into striated muscle cells, and form stable grafts at the site of damage or disease.

page 19, lines 20-31, wherein applicant discloses:

> As described above, the stem cells used according to the method of the invention are stem cells obtained from peripheral blood. These cells are capable of proliferating and differentiating into multiple muscle cell types, such as cardiomyocytes or skeletal myocytes. Stem cells for repopulating skeletal and cardiac muscle can be distinguished by their ability to form striated muscle cells in cell culture assays or by characteristic expression patterns of cell surface antigens, such as, but not limited to antigens reactive with SH2, SH3 and SH4 monoclonal antibodies (see US Patent NO. 5,486,359).

Claims 1, 5, 6, 10-14, 17, 18, 20, 22, 23, 27-31, 35, 37, 38, 42-44 and 45 stand rejected under 35 U.S.C. 102(b) for purportedly being anticipated by Kocher et al., "Neovascularization of ischemic myocardium by human bone marrow derived angioblasts prevents cardiomyocyte apoptosis, reduces remodeling and improves cardiac function", *Nature Medicine* (April 2001) Vol. 7, No. 4, pp 430-436 ("Kocher"). In view of the amendments to the claims and the following remarks, applicant respectfully requests that the Examiner reconsider and withdraw the rejection.

The Examiner states:

> the reference by Kocher et al. discloses a method of treating damaged or diseased tissue such as infracted myocardium wherein the method comprising steps of (a) isolating G-CSF mobilized CD 34^+ stem cells from peripheral blood of a human donor by apheresis....

Those of ordinary skill in the art appreciate that $CD34^+$ is a hematopoietic lineage marker and not a marker of non-hematopoietic cells capable of differentiating in multiple muscle cell types. Thus Kocher's method for treating damaged or diseased tissue depends on administering stem cells enriched for hematopoietic lineage cells to achieve neovascularization. In particular, Kocher isolates a population of stem cells that are enriched for endothelial precursors having the properties of hemangioblasts (page 430, right col.) for induction of vasculogenesis and

angiogenesis. Kocher does not teach, or suggest, a method for producing grafts of muscle tissue by isolating and administering stem cells to a subject in need thereof. As such, Kocher does not anticipate applicants' claims.

In view of the amendments to the claims and the forgoing remarks, applicants respectfully request that the Examiner reconsider and withdraw the rejection of the claims under 35 U.S.C. 102(b) for purportedly being anticipated by Kocher et al.

Claims 1, 9-14, 17, 18, 21, 26-31 and 41-45 stand rejected under 35 U.S.C. 102(b) for purportedly being anticipated by Kalka et al., "Transplantation of *ex vivo* expanded endothelial progenitor cells for therapeutic neovascularization," *PNAS* (March 28, 2000) Vol. 97, No. 7 pp 3422-3427. Kalka expands human peripheral blood mononuclear cells (PBMCs) in culture under conditions that produce a population of differentiating cells of the endothelial lineage. Kalka then transplants the endothelial cell precursors into mice with hindlimb ischemia and assays for blood flow recovery and capillary density (p. 3424, right col.). Kalka does not teach or suggest a method for producing grafts of muscle tissue by isolating and administering stem cells to a subject in need thereof. As such Kalka does not teach or suggest applicants invention as claimed.

In view of the amendments to the claims and the foregoing remarks, applicant respectfully requests that the Examiner reconsider and withdraw the rejection of the claims under 102(b) in view of Kalka.

Claims 1-45 stand rejected under 35 U.S.C. 103(a) for purportedly being unpatentable over the combination of Kocher, Kalka and Lagasse et al., "Purified hematopoietic stem cells can differentiate into hepatocytes in vivo," *Nature Medicine* (November 2000) Vol. 6, No. 1, pp. 1229-1234("Lagasse"). Applicants respectfully disagree.

As discussed *supra*, both Kocher and Kalka disclose methods for neovascularization and do not teach or suggest a method for producing a graft of muscle tissue by isolating and administering stem cells to a subject in need thereof. Lagasse does not compensate for the deficiencies of Kolcher and Kalka. Lagasse also fails to teach or suggest a method for producing grafts of muscle tissue by isolating and administering stem cells. Without such a teaching or

suggestion one of skill in the art would not be motivated based on Kolcher, Kalka or Lagasse alone or in combination, to develop a method such as that presently claimed by applicant.

In view of the amendments to the claims and the foregoing remarks applicant respectfully request that the Examiner reconsider and withdraw the rejection of the claims under 35 U.S.C. §103(a) in view of Lagasse, Kocher and Kalka.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

If additional fees are due, please charge our Deposit Account No. 50-0624, under Order No. WO-BSX 233/10408840 from which the undersigned is authorized to draw.

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Respectfully submitted,

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